

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
2 June 2005 (02.06.2005)

PCT

(10) International Publication Number  
**WO 2005/049600 A1**

(51) International Patent Classification<sup>7</sup>: **C07D 401/04**,  
A61P 25/00, A61K 31/4439

(21) International Application Number:  
PCT/EP2004/012772

(22) International Filing Date:  
10 November 2004 (10.11.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
0326407.4 12 November 2003 (12.11.2003) GB

(71) Applicant (for all designated States except US): **GLAXO GROUP LIMITED** [GB/GB]; Glaxo Wellcome House, Berkeley Avenue, Greenford Middlesex UB6 0NN (GB).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **ALVARO, Giuseppe**

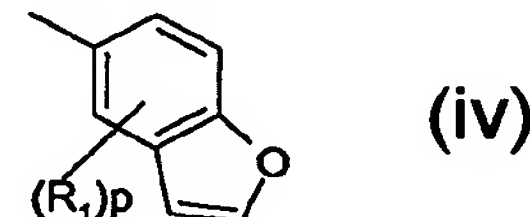
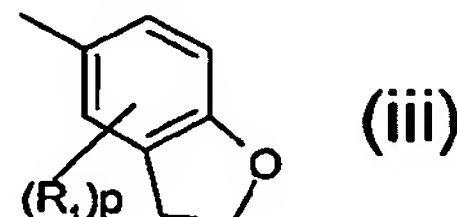
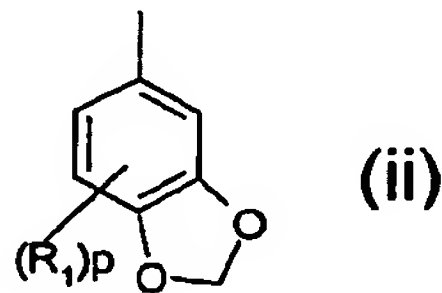
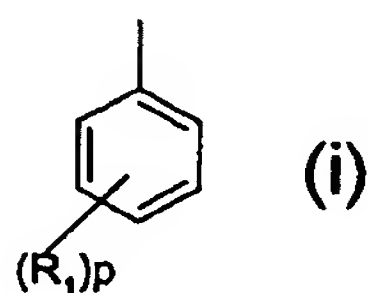
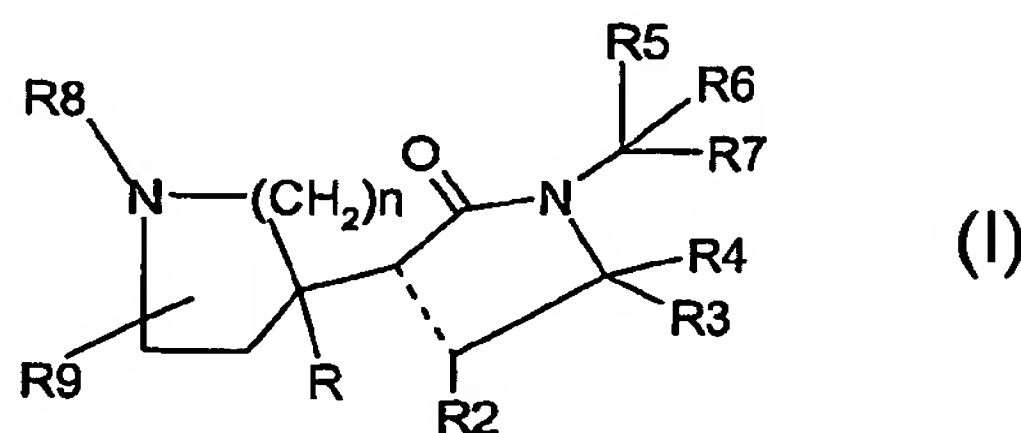
[IT/IT]; GlaxoSmithKline, Via Alessandro Fleming 2, I-37100 Verona (IT). **DI FABIO, Romano** [IT/IT]; GlaxoSmithKline, Via Alessandro Fleming 2, I-37100 Verona (IT). **GIOVANNINI, Riccardo** [IT/IT]; GlaxoSmithKline, Via Alessandro Fleming 2, I-37100 Verona (IT). **PAIO, Alfredo** [IT/IT]; GlaxoSmithKline, Via Alessandro Fleming 2, I-37100 Verona (IT). **TRANQUILLINI, Maria, Elvira** [IT/IT]; GlaxoSmithKline, Via Alessandro Fleming 2, I-37100 Verona (IT). **MATTIOLI, Lucia** [IT/IT]; GlaxoSmithKline, Via Alessandro Fleming 2, I-37100 Verona (IT).

(74) Agent: **GIDDINGS, Peter, John**; GlaxoSmithKline, 980 Great West Road (CN925.1), Brentford, Middlesex TW8 9GS (GB).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,

[Continued on next page]

(54) Title: BETA-LACTAMS FOR TREATMENT OF CNS DISORDERS



(57) Abstract: The present invention relates to novel compounds of formula (I) wherein ---- represents a single or a double bond; R represents a radical selected from formulae i), ii), iii) and iv) in which R<sub>1</sub> is halogen, cyano, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkoxy, trifluoromethyl or trifluoromethoxy and p is zero or an integer from 1 to 3; R<sub>2</sub> represents hydrogen or C<sub>1-4</sub> alkyl; R<sub>3</sub> represents hydrogen, hydroxy or C<sub>1-4</sub> alkyl; R<sub>4</sub> represents hydrogen or R<sub>4</sub> together with R<sub>3</sub> represents =O or =CH<sub>2</sub>; R<sub>5</sub> represents phenyl, naphthyl, a 9 to 10 membered fused bicyclic heterocyclic group or a 5 or 6 membered heteroaryl group, wherein said groups are optionally substituted by 1 to 3 groups independently selected from trifluoromethyl, C<sub>1-4</sub> alkyl, hydroxy, cyano, C<sub>1-4</sub> alkoxy, trifluoromethoxy, halogen or S(O)<sub>q</sub>C<sub>1-4</sub> alkyl; R<sub>6</sub> and R<sub>7</sub> independently represent hydrogen, cyano, C<sub>1-4</sub> alkyl; R<sub>8</sub> is (CH<sub>2</sub>)<sub>r</sub>R<sub>10</sub>; R<sub>9</sub> represents hydrogen, halogen, C<sub>3-7</sub> cycloalkyl, hydroxy, nitro, cyano or C<sub>1-4</sub> alkyl optionally substituted by one or two groups selected from halogen, cyano, hydroxy or C<sub>1-4</sub> alkoxy; R<sub>10</sub> represents hydrogen or C<sub>3-7</sub> cycloalkyl; n represents 1 or 2; q is 0, 1 or 2; r is 0 or an integer from 1 to 4; or a pharmaceutically acceptable salt or a solvate thereof, process for their preparation and their use in the treatment of conditions mediated by tackykinins and/or by selective inhibition of the serotonin reuptake transporter protein.



TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Declarations under Rule 4.17:**

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)
- of inventorship (Rule 4.17(iv)) for US only

**Published:**

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.